

THIN-FILM PERIPHERAL NERVE ELECTRODE

Tri-Annual Progress Report
Covering Period September 27, 1993 to January 31, 1994
CONTRACT NO. N44-NS-3-2367

**S. F. Cogan
M. McCaffrey**

**EIC Laboratories, Inc.
111 Downey Street
Norwood, Massachusetts 02062**

and

**Hines VA Hospital
Rehabilitation R&D Center
Hines, Illinois 60141**

Prepared for

**National Institutes of Health
National Institute of Neurological
Disorders and Stroke
Bethesda, Maryland 20892**

April 12, 1994

TABLE OF CONTENTS

<u>Section</u>		<u>Page</u>
1.0	BACKGROUND.....	3
2.0	TECHNICAL PROGRESS	4
3.0	ANIMAL STUDIES	9

1.0 BACKGROUND

A program to develop a FNS system capable of graded and stable activation of hand muscles for the restoration of grasp in quadriplegic individuals has been proposed. The objective of the program is the development of a thin film neural cuff electrode and the demonstration of the efficacy of the electrode for grasp in an *in vivo* study using a raccoon model.

Specific features of the proposed electrode include:

- multiple, independently addressable charge injection sites that will facilitate implementation of established and emerging stimulation protocols such as anodal field steering and anodal blocking;
- leads and electrodes are vacuum deposited on a planar, monolithic fluorocarbon substrate that is flexible and avoids bulky interconnects in close proximity to the implantation site;
- charge injection electrodes of Pt or anodized iridium oxide (AIROF), both of which are stable under the anticipated charge injection protocols;
- fluorocarbon substrates (FEP Teflon®) that can be thermoformed into a self-sizing cuff to allow a snug but elastic fit to the nerve.

The circumneural electrodes are fabricated by vacuum depositing metal films on thin sheets of fluorocarbon polymer and photolithographically patterning the leads and charge injection sites. The patterned substrate is then thermally sealed with a second polymer layer to electronically isolate the leads from the physiological environment. The charge injection sites are exposed by a combination of photolithography and ion or plasma etching of vias through the polymer overlayer. Once all planar fabrication processes, i.e., photolithography, vacuum deposition, and etching have been completed, the electrode is cut out of the substrate and the desired cuff and lead geometries created by thermoforming.

An example of an electrode in planar geometry prior to thermoforming the cuff is shown in Figure 1. The leads and charge injection sites are patterned on a large polymer substrate with the leads extending to a bonding pad that is located a significant distance proximal to the cuff. Four charge injection sites, in a "round about" geometry, similar to that being investigated for phrenic nerve stimulation (Baer *et al.*, 1990), are shown on the cuff. Optional perforations through the cuff and a suturing tab are also indicated.

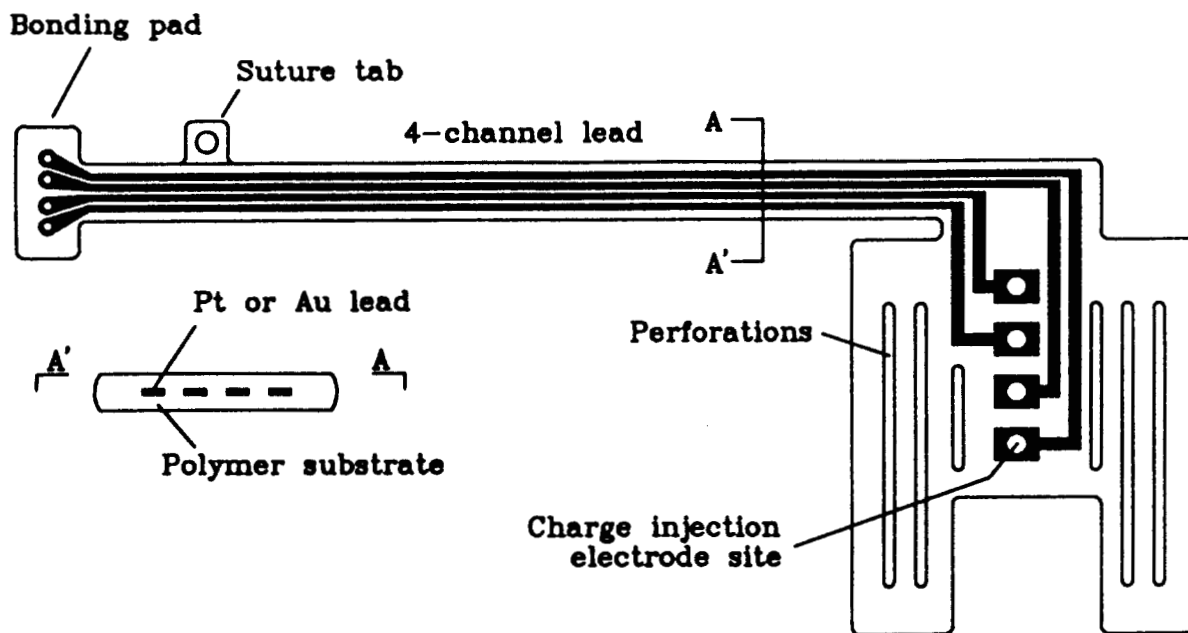


Figure 1. A circumneural cuff having four "round about" charge injection sites, perforations, interconnect bonding pad, and suture tab.

Recent studies suggest that selectivity and gradation are possible with cuff or helical nerve electrodes when sufficient latitude in the number and geometry of charge injection sites is provided (Baer *et al.*, 1990; Fang and Mortimer, 1991a,b). Electrode designs or stimulation protocols that might be employed with cuff electrodes include: monopolar from a single or multiple sites with the implanted stimulator as the indifferent electrode; six position "round about" stimulation at two locations; bipolar between longitudinal and transverse electrode pairs; anodal blocking; collision blocking; and combinations of these. The anodal field steering technique recently demonstrated on the cat sciatic nerve by Sweeney *et al.* (1990) may be particularly appropriate for grasp using the median nerve because of the general similarity in fascicular localization between these nerves.

2.0 TECHNICAL PROGRESS

The objectives of the first trimester of the program have been the refinement of electrode fabrication methods at EIC Laboratories and facilities preparation and development of experimental protocols for acute studies in the raccoon model at the Hines Rehabilitation Research and Development Center.

2.1 Electrode Fabrication

Optimization of Vacuum Deposition Conditions

Task I involved optimization of vacuum deposition conditions for multilayered, thin film, metallization on thin, Teflon[®] substrates. In Phase I, satisfactory results were obtained with sputter deposited metallization for both lead and Ir charge injection sites. These coatings were adherent and electrically conductive after steam sterilization and prolonged immersion in PBS at 90°C. However, microfracturing of the metallization, probably associated with residual stresses during sputtering, has been observed. Several approaches to eliminating the microfracturing have been taken. These approaches include: reduction of the applied RF bias during deposition of the initial Ti adhesion layer; rotation of the planet on which the substrates are mounted during deposition to minimize heating and bombardment by energetic species; and compositional grading of interfaces between the individual metal films in the coating.

Deformation of the Teflon[®] substrates due to relaxation of residual stresses or stress induced during sputtering was prevented by mounting the substrates on ITO-coated glass (ITO is a thin optically transparent electrically conductive film of tin-doped indium oxide). The Teflon[®] was fixed to the glass using double-sided adhesive tape and a UV-polymerizable acrylic adhesive to produce the structure

glass/ITO/acrylic adhesive/adhesive-tape/FEP Teflon[®].

The acrylic is a non-solvent, optical adhesive which cures when irradiated by ultraviolet light. This structure maintains its integrity during heat treatment at temperatures of >100°C and tolerates immersion in all chemical baths used in our positive-resist photolithography process. Plasma irradiation during sputtering also has no deleterious effects over the comparatively short exposure periods. The metallized FEP Teflon[®] substrates are easily detached from the adhesive tape by soaking in acetone. Any residual adhesive can be removed by gently rubbing the back surface of the cuff electrode with soft cloth aids.

Non-uniform film deposition, due to the comparatively small diameter (5 cm) of the sputter targets compared with the cuff electrode area is compounded by the effects of substrate biasing. The Ti adhesion layer must be deposited with an RF bias applied to the substrate to ensure adhesion to the FEP Teflon[®]. Since an RF electrical connection presently precludes obtaining uniform film deposition by rotating the planet on which the substrates are mounted, an oscillatory motion was investigated as an alternative. By rocking the planet underneath the Ti target during deposition, the substrates are evenly coated and the non-uniformity minimized. Insulated wires

can be connected directly to the ITO coating on the glass to provide an RF bias without need for a rotating electrical contact. The oscillatory motion is obtained by driving the planet with computer controlled stepper motor.

Previously, both the Ti adhesion layer and Ir electrode layer had been deposited with an applied bias to increase adhesion between the Ti and Ir films. Since prolonged deposition with a bias causes excessive heating of the substrate, compositional grading of the Ti-Ir interface was investigated. The interface is graded by sputtering simultaneously from two targets and systematically increasing the sputtering current at one target and decreasing it at the other, while maintaining the total current constant. The planet with the Teflon[®] substrates is spun underneath the two targets during deposition at a speed of ~100 rpm to ensure uniform coating. Details of the deposition processes are provided in Table 1.

The as-deposited Ti-Ir layers are specular and uniform in appearance. The metallization passes an initial tape test and also after autoclaving for 30 minutes at 120°C. Although the films do not pass the tape test after overnight soaking in PBS at 90°C, a Ti-Ir sample soaking at 37°C in PBS has passed the tape test after 9 weeks. This test is continuing. The occurrence of microcracking has been significantly reduced although, when it does occur, the cracks that do form are wide enough and deep enough to significantly hinder current flow and increase sheet resistivity. A scanning electron micrograph of a typical microfractured structure is shown in Figure 2. We will continue to investigate this problem in the next trimester of the project.

Patterning Metallization

Photolithography is required to define the metallization for the charge injection sites and the conductive traces leading to these sites. In phase I, conditions for the lift off process in which metal is deposited over patterned photoresist and subsequently removed by stripping were established. Prior to applying the photoresist, the Teflon[®] films are cleaned by washing in a 2:1 mixture of concentrated H₂SO₄ and H₂O₂ (30%) and exposure to an oxygen plasma for 15 minutes. Shipley 1800 positive photoresist is then spun on the FEP Teflon[®] at 3500 rpm for 25 seconds and soft baked at 100°C for 30 minutes. Photoresist is exposed through a Cr mask using an Oriel UV exposure and mask alignment system. Following UV exposure the resist was developed in Shipley CD-30 developer and rinsed in distilled water. Figure 3 shows Ti/Ir/Au three-layer metallization deposited on 0.003 inch thick FEP Teflon[®] using the liftoff process.

Table 1. Deposition conditions for Ti-Ir layers on FEP Teflon®.

Global Parameters:

pressure:	10 microns
gas flow rate:	Argon, 10 sccm
target-to-substrate distance:	6cm
DC power to magnetron	47 watts (310 V DC)
RF power for substrate biasing	5 watts

Layer 1: Ti Adhesion Layer

applied bias:	-80V
current control:	150mA
balancing voltage:	310V
time:	6 minutes
approximate thickness of Ti:	25 nm

Layer 2: Graded Interface

applied bias: 0

<u>Ti mA</u>	<u>Ir mA</u>	<u>time minutes</u>
150	0	4
130	30	1
110	50	1
90	70	1
70	90	1
50	110	1
30	130	1

approximate thickness of graded interface: 45 nm

Layer 3: Iridium

applied bias:	0
current control:	150 mA
target voltage:	442 V
time:	6 minutes

approximate thickness Ir:	35 nm
---------------------------	-------

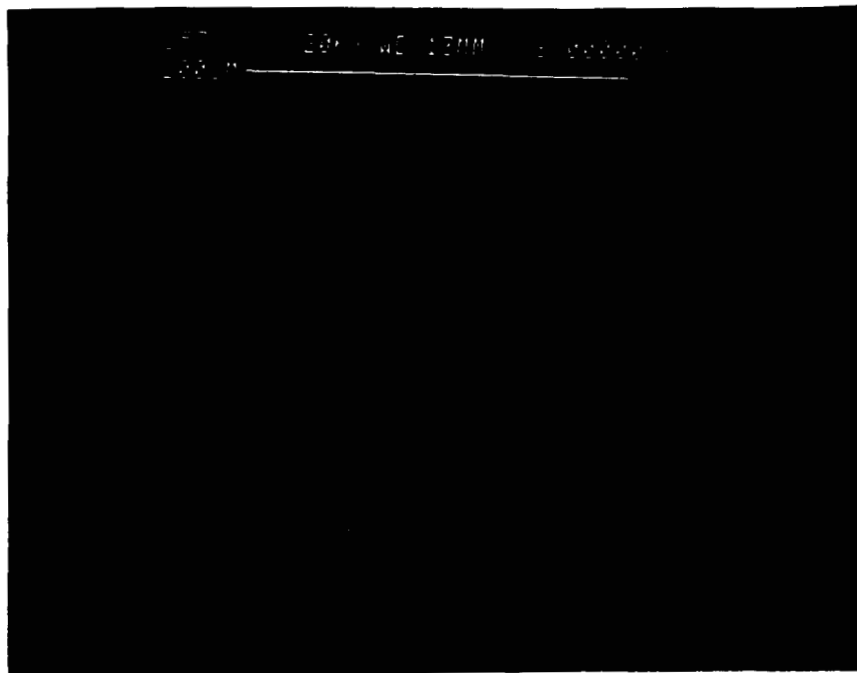


Figure 2. Scanning electron micrograph of microfracturing in sputtered metallization on FEP Teflon®.



Figure 3. Scanning electron micrograph of three-layer Ti-Ir-Au metallization on FEP Teflon®.

Passivation and Insulation

A patterned insulating layer is required on the internal surface of the cuff to define the charge injection sites and isolate the electrical leads from the physiological electrolyte. Primary requirements of the insulation are good barrier properties to prevent ion and H₂O transport, low electronic conductivity, flexibility, and adhesion to the metals and Teflon®. Teflon® AF, a fluorocarbon polymer dissolved in a perfluoroalkyl solvent, is being used initially for this application. The polymer solution is spun onto the metallized and patterned substrates and thermally annealed to remove solvent. Typical process conditions for the Teflon® AF coatings are provided in Table 2.

Table 2. Coating conditions for Teflon® AF films on metallized FEP Teflon®.

solution mixture:	weight ratio 2:1 Teflon® AF(18% by weight): Fluorinert solvent
spin speed:	1500 rpm
spin time:	60 seconds
thermal annealing:	
1. air set:	5-7 minutes
2. bake 112°C:	5-7 minutes
3. bake 170°C:	temperature ramped from 112C to 170C in 20 minutes, held 170°C for 10 minutes.

Sample is cooled and given a second coat of Teflon® AF. Heat treatment is repeated. After steps 1-3, the temperature is ramped from 170°C to 240°C in 20 minutes and held at 240°C for 10 minutes.

The two-layer Teflon® AF coatings are smooth and flexible. Leakage current measurements have shown them to be good barriers to ion and H₂O transport. The coatings have remained adherent to FEP Teflon® after 8 weeks in both 90°C and 37°C PBS test solutions. These results are in contrast to results obtained for Teflon® AF films on Si substrates for which delamination occurs rapidly under these conditions (Thin Film Hermetic Coatings, Fifth Quarterly Report, NINDS Contract No. N44-NS-2-2311).

Etching to Expose Charge Injection Sites

The charge injection sites are also coated with the Teflon[®] AF insulation which must be removed from these sites by chemical or plasma etching. It was found that the Teflon[®] AF could be plasma etched in a PECVD system using an O₂:CF₄ plasma without damaging the metallization or cuff structure. A 1/16" metal mask was used to cover the cuff electrode and expose 1 mm diameter injection sites. Conditions used to etch the Teflon[®] AF are reported in Table 3.

Table 3. Conditions for plasma etching Teflon[®] AF.

Etching Gas:	92%O ₂ :8%CF ₄
Pressure:	500 millitorr
Temperature:	150°C
RF Power:	200 Watts
Time:	20 minutes

Thermoforming

The metallized and insulated cuff is cut to appropriate planar shape. The cuff is then thermoformed to the desired diameter and overlapped by rolling into a tube, inserting in an aluminum mold with various diameter tube slots, and annealing at 270°C for 30 minutes. The resulting cuff is permanently curled in a cylindrical shape with diameters ranging from 2.8 mm to 3.6 mm and with an overlap of about 33%.

Electrode Design

The design of an electrode suitable for acute animal studies has been completed. An overview of this electrode is shown in Figure 4. The electrode has four charge injection sites - a longitudinal tripole and steering electrode. The tab with the metal leads is oriented perpendicular to the longitudinal axis of the nerve to facilitate interconnection and routing. Photolithograph masks for this electrode have been procured and several prototype electrodes fabricated. A different design will be used for chronic studies.

CUFF 1, November 1993

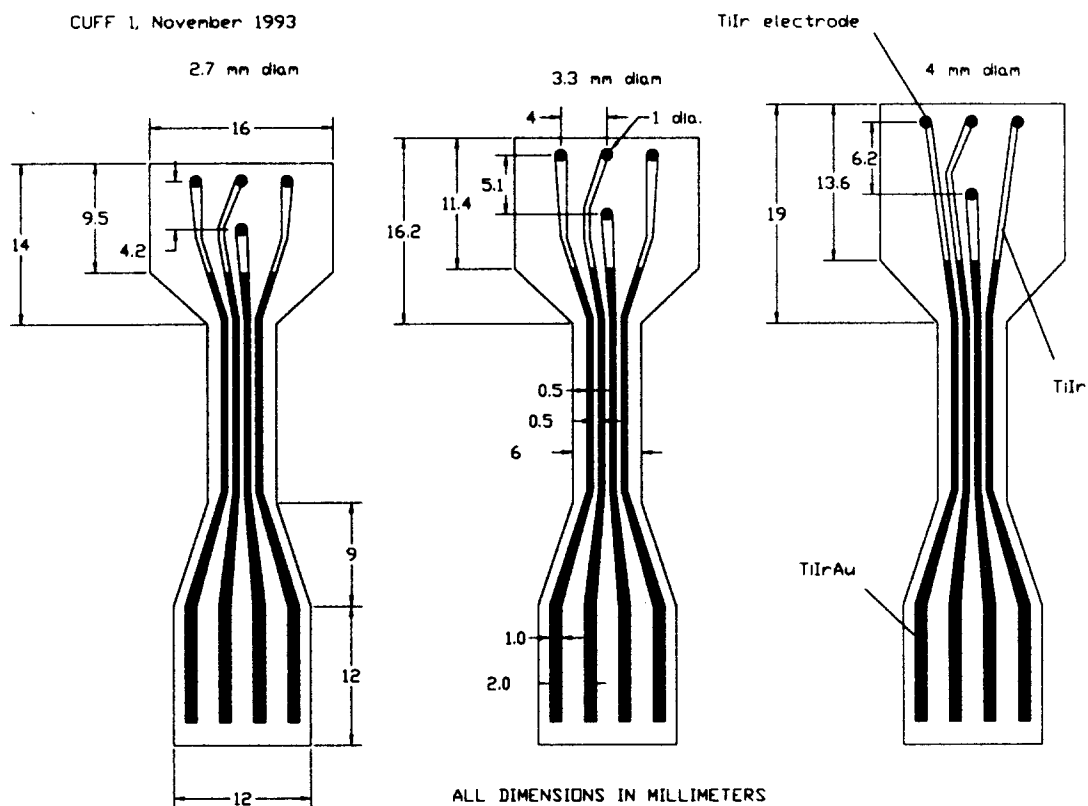


Figure 4. Design of a four-electrode cuff for acute animal studies.

3.0 ANIMAL STUDIES

The following section contains the report from the Hines VA Hospital, Rehabilitation R&D Center, for the animal studies portion of the program.

**Progress Report #1: Thin-Film Peripheral Nerve Electrode
for Subcontract: *In vivo* Studies, SBIR Topic 13**

Submitted to: Dr. Stuart Cogan, Head of Material Science

EIC Laboratories, Inc.

From: James S. Walter, Ph.D.; Charles Robinson, D.Sc.; James Sweeney, Ph.D.;
Jerry McLane, Ph.D.; Paul Zaszcsurynski, B.S.; Wuying Cai, M.D.;
Mike Bidnar, M.D.; Talat Khan. Ph.D.

Hines VA Hospital, Rehabilitation R&D Center, Hines, IL 60141

Abstract

We have proposed that complex hand movements might be obtained with direct median nerve stimulation through an implanted multielectrode nerve cuff. We expect to show that selective stimulation can induce activation of digits and induce a graded response in digits. In addition, the direct nerve stimulation should induce repeatable hand responses and result in no injury to the nerve.

Progress

A. Animal Model. Animals are on order and will be delivered early in February. Dissection of two cadaver raccoon forearms indicates that the muscles of the forearm are similar to humans. Major digit flexors such as flexor digitorum superficialis and flexor digitorum profundus, and extensor muscle of the digits the extensor digitorum communis have the same functions in humans and raccoons. The thumb flexor muscle, the flexor pollicis longus and the major extensor muscle, the extensor pollicis longus are also in the same location in both species. The wrist flexor (Flex. carpi radialis, flexor carpi ulnaris) and extensor (extensor carpi radialis, extensor carpi ulnaris) are also in the same relative locations.

Selective responses of forearm muscles to median nerve stimulation will depend upon the structure of the median nerve. We observed clear fascicular demarcations in the median nerve within the upper arm of the raccoon. We could trace many of these fascicles to specific muscles. Thus, selective activation of one or two muscles should be possible using graded stimulation. Because of marked fasciculation we should also expect that we could activate different muscles with stimulation in different quadrants of the nerve.

The raccoon median nerve is easily accessible within the upper forearm. It courses for a short length within the upper arm close to the skin giving easy access for our nerve cuff.

B. Cuff Construction. The two raccoon median nerves that we inspected were about 3 mm by 4 mm in diameter. We have evaluated four different nerve cuff constructions in the cadaver. A cuff with the inside diameter approximately equal to the nerve was found to have the best fit. The cuff that wrapped one and a half times around the nerve appears to be the best based on ease of application and ability to remain secure around the nerve.

C. Methods for Evaluating EMG, Paw and Digit Movement. Considerable effort has been extended during this project period in developing recording techniques. A recording platform has been constructed in our model shop that will hold the arm and allow free digit movement. Force transducers have been procured and connected to our recording system. EMG recording systems have been set up. The implantable stimulator has been ordered for connecting to the 12 electrode cuff electrode.

3.0 FUTURE WORK

In the next trimester, we will continue with the refinement of deposition processes to further improve adhesion and electrical conductivity of Ti/Ir and Ti/Ir/Au films on FEP Teflon®. Electrodes for acute studies will be sent to Hines for *in vitro* evaluation of charge injection using the implantable stimulator purchased by Hines for animal studies. Protocols for activation of the Ir charge injection sites and extended testing of the stability of the AIROF films is currently underway and will be described in the next report.

The limits of our photolithographic processing on FEP Teflon^R films are currently being explored with a view to fabricating cuff electrodes for other contractors in the NINDS program. Our goal will be to achieve metallization line widths and interline spacings of less than 100 µm.

A problem facing the eventual application of these electrodes in clinical studies is the unwillingness of the manufacturer of Teflon® AF, the DuPont Company, to permit chronic, implanted application of this product in human patients. DuPont also refuses to supply Teflon® AF to research groups doing biomedical research involving chronic implantation. For this reason, we are obliged to consider alternatives. Other spun polymer films such as polyesterimides that can be processed in much the same way as Teflon AF® are now being investigated.

References

- Baer, G.A., Telomen, P.P., Shaneerson, J.M., Markkula, H., Exner, G., And Wells, F. (1990) "Phrenic nerve stimulation for central ventilatory failure with bipolar and four pole electrode systems," *Pace*, 13:1061-1072.

- Fang, Z. -P., Mortimer, J. T. (1991a) "Selective activation of small motor axons by quasitrapezoidal current pulses," IEEE Trans. Biomed. Eng., **38**:168-174.
- Fang, Z. -P., Mortimer, J. T. (1991b) "A method to effect physiological recruitment order in electrically activated muscle," IEEE Trans. Biomed. Eng. **38**:175-179.
- Sweeney, J. D., Ksienski, D. A., And Mortimer, J. T., (1990) "A nerve cuff technique for selective excitation of peripheral nerve trunk regions," IEEE Trans. Biomed. Eng. **37**:706-715.